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Associations between Long-Term Air Pollutant Exposures and Blood Pressure in Elderly Residents of Taipei City: A Cross-Sectional Study

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Short-running title: Long-term air pollution and blood pressure

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Abstract

Background: Limited information is available regarding long-term effects of air pollution on blood pressure (BP) and hypertension. We studied whether one-year exposures to particulate matter (PM) and nitrogen oxides were correlated with BP and hypertension in the elderly.

Methods: We analyzed cross-sectional data from 27,752 Taipei City residents over 65 years of age who participated in a health examination program in 2009. Land-use regression models were used to estimate participants' one-year exposures to particulate matter with aerodynamic diameter <10 μm (PM_{10}), coarse particles ($PM_{2.5-10}$), fine particles ($PM_{2.5}$), $PM_{2.5}$ absorbance, nitrogen oxides (NO_x), and nitrogen dioxides (NO_2). Generalized linear regressions and logistic regressions were used to examine the association between air pollution and BP and hypertension, respectively.

Results: Diastolic BP was associated with one-year exposures to air pollution, with estimates 0.73 [95% confidence interval (CI): 0.44, 1.03], 0.46 (95% CI: 0.30, 0.63), 0.62 (95% CI: 0.24, 0.99), 0.34 (95% CI: 0.19, 0.50), and 0.65 (95% CI: 0.44, 0.85) mmHg for PM_{10} (10 $\mu g/m^3$), $PM_{2.5-10}$ (5 $\mu g/m^3$), $PM_{2.5}$ absorbance ($10^{-5}m^{-1}$), NO_x (20 $\mu g/m^3$), and NO_2 (10 $\mu g/m^3$), respectively. $PM_{2.5}$ was not associated with diastolic BP, and that none of the air pollutants was associated with systolic BP. Associations of diastolic BP with PM_{10} and $PM_{2.5}$ absorbance were stronger among participants with hypertension, diabetes, or a body mass index $\geq$ 25 kg/m^2 than among participants without these conditions. One-year air pollution exposures were not associated with hypertension.

Conclusions: One-year exposures to PM_{10}, $PM_{2.5-10}$, $PM_{2.5}$ absorbance, and nitrogen oxides were associated with higher diastolic BP in elderly residents of Taipei.

Introduction

The 2010 American Heart Association (AHA) scientific statement on particulate air pollution asserts that increased arterial blood pressure (BP) is an important outcome of acute particulate matter (PM) exposures and a possible biological mechanism linking PM exposure to cardiovascular disease (Brook et al. 2010). However, less is known about the role of long-term PM exposures on BP. Several studies have investigated the impacts of long-term PM exposures with respect to BP (Auchincloss et al. 2008; Chuang et al. 2011; Fuks et al. 2011; Schwartz et al. 2012; Sørensen et al. 2012; Dong et al. 2013; Fuks et al. 2014; Liu et al. 2014); however, the results remain inconclusive. An epidemiological study first reported that average 30-day exposures to fine particles ($PM_{2.5}$) were positively associated with pulse pressure and systolic BP (Auchincloss et al. 2008). Epidemiological studies in Europe and the U.S. further reported that average one-year exposures to $PM_{2.5}$ or black carbon were positively associated with both systolic and diastolic BP (Fuks et al. 2011; Schwartz et al. 2012). Additionally, two cross-sectional studies in Asian countries found positive associations between long-term exposure to PM and increased BP and hypertension (Chuang et al. 2011; Dong et al. 2013). However, reported associations between air pollution and BP have differed among studies, possibly due to differences in characteristics among study cohorts. For example, a Danish cohort found that one- and five-year exposures to nitrogen oxides (NO_x), a traffic-emitted indicator, were associated with a decrease in BP among middle-aged subjects (Sørensen et al. 2012), while Liu et al. (2014) reported no associations between long-term traffic-related air pollution exposures and BP in children aged 10 years. The largest multicenter study to date by Fuks et al. (2014) used 15 population-based cohorts, participating in the European Study of Cohorts for Air Pollution Effects (ESCAPE), to investigate the effects of residential exposures to PM and

nitrogen oxides on BP and prevalent hypertension in European populations. They reported that systolic and diastolic BP in non-antihypertensive medicated participants were associated with traffic load on major roads within 100 m of residence, but not with concentrations of air pollutants modelled by land use regression (LUR). The odds ratio for prevalent hypertension was also elevated with traffic load (Fuks et al. 2014).

The inconsistent findings of associations between long-term exposures to air pollution and BP may be attributed to the heterogeneity of PM sizes or compositions between study locations. Some studies have shown that the BP was positively associated with PM in the presence of roadway traffic or traffic-related particles (Auchincloss et al. 2008; Schwartz et al. 2012; Fuks et al. 2014). Differences in exposure measurements also may contribute to diverse findings on associations between PM and BP among studies. The use of fixed-site monitoring data to assess residential PM exposures, as described in the studies by Auchincloss et al. (2008), Chuang et al. (2011), and Dong et al. (2013), most likely result in the misclassification of exposures that can eventually bias the research findings. LUR models have been successfully applied in the ESCAPE project to model residential long-term air pollution on a small spatial scale to a spatial resolution of 25 m, reflecting within-city differences in traffic-related emissions among European cities (Eeftens et al. 2012; Wang et al. 2013). In this study, we applied the LUR model based on the ESCAPE protocol to estimate one-year exposures to different sizes and compositions of air pollution, including particulate matter with aerodynamic diameter <10 μm (PM_{10}), coarse particles ($PM_{2.5-10}$), $PM_{2.5}$, $PM_{2.5}$ absorbance, NO_x, and nitrogen dioxides (NO_2), and investigated whether BP and hypertension were associated with these air pollutants in elderly participants living in Taipei City.

Materials and Methods

Study Population. We used a cross-sectional design in this study and the study population was selected from the Taipei City Elderly Health Screening Program in 2009 (http://www.gov.taipei/ct.asp?xItem=1098183&ctNode=5321&mp=100001). This program is an annual program run by the Department of Health of Taipei City Government from March 1st to August 31st. All senior citizens over the age of 65 years old and residing in Taipei City, are invited to participate in this health screening program every three years. The Department of Health of Taipei City Government prepared a data set, which has been decoded and delinked personal information of names and IDs from medical record, for medical research. We were allowed to use this data for our study after our application for use has been approved by Department of Health of Taipei City Government. Overall, 42,105 participants participated in this program in 2009. After excluding 11,666 participants with missing information on variables used in the analysis or used to estimate exposure, 30,439 participants were candidates for this study. Using the validation data from electronic sphygmomanometers (Christofaro et al. 2009), subjects whose measured BP values were higher than 190 mm Hg or lower than 90 mm Hg for systolic BP and higher than 120 mm Hg or lower than 60 mm Hg for diastolic BP were further excluded to minimize the potential for measurement errors in BP values. This gave us a final total of 27,752 subjects recruited for this study. This study was approved by the Joint Institutional Review Board of the Public Health College of the National Taiwan University.

Health assessment. The health screening program was conducted in 10 branches of the Taipei Municipal Hospital and consisted of a clinician interview, self-reported questionnaire, and

venous biochemistry sampling. The clinician interview record and questionnaire provided information including home address, age, sex, height, weight, body mass index (BMI), education level, smoking status, alcohol consumption, betel-nut-chewing status, and physical activity, as well as a history of physician-diagnosed hypertension and diabetes for each subject.

The study subjects' BP measurements, i.e., systolic and diastolic BP, were taken by trained medical personnel using electronic sphygmomanometers (Model HEM-770A; Omron Health Care). All BP measurements were performed in the morning (0800 h to 1000 h). Following completion of the 30-minute questionnaire interview, BP was measured once in a seated, upright position. One of three cuff sizes (adult standard, large, and thigh-sized) was used depending on the circumference of the subject's left upper arm. To minimize the potential effects of anti-hypertensive drugs, participants were instructed to not take any medication the morning of the BP measurement. In this study, subjects who either had a self-reported physician-diagnosed hypertension (subjects had been diagnosed with hypertension and use of anti-hypertensive medication) or had measured unknown hypertension (measured BP values equal to or higher than 140 mm Hg for systolic BP or 90 mm Hg for diastolic BP but had never been diagnosed with hypertension) were all defined as hypertensive subjects.

Exposure assessment. We used the LUR to model the annual average concentrations of different sizes and compositions of air pollution, including PM_{10}, $PM_{2.5-10}$, $PM_{2.5}$, $PM_{2.5}$ absorbance, NO_x, and NO_2, for each participant. This modeling approach was derived and developed from the ESCAPE project (http://www.escapeproject.eu/manuals) (Eeftens et al. 2012; Wang et al. 2013). In summary, NO_x and NO_2 were measured for three 14-day periods during intermediate season (October to December 2009), cold season (January to March 2010),

and warm season (June to August 2010) at 40 spatially distributed sampling sites in Taipei. The average temperature and relative humidity were 21.0 ºC and 76%, 18.2 ºC and 78%, and 28.8 ºC and 74% for the three seasons, respectively. Ogawa passive badges (Ogawa USA, Inc.) were used to measure NO_x and NO_2 concentrations at urban backgrounds and streets. $PM_{2.5}$ and PM_{10} were measured at 20 of the 40 sampling sites using Harvard impactors (Air Diagnostics and Engineering Inc.). The collected filters were then measured using Smoke Stain Reflectometer (Model 43, Diffusion Systems Ltd.) to determine $PM_{2.5}$ absorbance. Land use data and traffic-related information were combined with measured concentrations to derive LUR models using supervised forward stepwise multiple regressions. For traffic variables, circular buffers with radii of 25, 50, 100, 300, 500, and 1000 m around each site were calculated. For land use and population, buffers of 100, 300, 500, 1,000, and 5000 m were calculated. Different road types, including major roads (national highway, provincial highway, expressway, and city street), elevated highway (roads established above ground level or highway ramp), as well as all roads, were considered in LUR models. The fit of the final LUR models for each of the traffic-related air pollutants were good, with cross-validated R^2 values of 0.74, 0.52, 0.91, 0.92, 0.75, and 0.63 for PM_{10}, $PM_{2.5-10}$, $PM_{2.5}$, $PM_{2.5}$ absorbance, NO_x, and NO_2, respectively. Exposure modeling for NO_x and NO_2 followed the procedure outlined in Lee et al. 2014, and the statistics for land use variables are summarized in the supplemental material (See Supplemental Material, Table S1). Each participant's annual average exposures to the six air pollutants were calculated by inserting the values of the land use variables at their residential addresses into our LUR models.

Statistical analyses. ArcGIS (ESRI) was used to obtain Geographic Information System (GIS) information used in the air pollution exposure modeling. Generalized linear regression models

were applied to examine associations between one-year exposures to air pollutants and BP in elderly persons over the age of 65**.** We applied the variable selection technique, 10% change-in-estimate criterion (Rothman et al. 2008), to select potential confounding factors. In addition, the mean-centered square terms of continuous variables were included in the modeling if non-linearity is present checked by a scatter plot between the response variable and the predictor. The covariates of sex, age, age mean-centered square, BMI (body weight divided by the square of height measured at the health exam), BMI mean-centered square, smoking status (current smoker or non-current smoker), alcohol consumption (<1 drink/week, 1 to 3 drinks/week, or >3 drinks/week), education (primary school or less, up to secondary school or equivalent, or university degree or more), hypertension (classified as physician-diagnosed hypertension or measured unknown hypertension), and diabetes (subjects had been diagnosed with diabetes and use of anti-diabetic medication or fasting glucose over 126 mg/dl in the health examination), were finally identified as adjustment variables in the main model. In the extended model, we further adjusted for traffic proximity (distance to the nearest major road) in addition to the selected individual covariates in the main model to consider the possible effect of traffic noise. To account for the influence of individual comorbidities, analyses were performed to examine whether the association between BP and air pollution was modified by hypertension, diabetes, or obesity (BMI $\geq$ 25 kg/m^2). We also estimated associations stratified according to a history of physician-diagnosed hypertension versus no previous diagnosis of hypertension in addition to stratifying on hypertension (including measured but not diagnosed) versus no hypertension. We examined the effect modification in the regression models by including interaction terms between air pollution and individual comorbidity category.

We used logistic regression models to estimate associations between one-year average exposures to air pollutants and prevalent hypertension, with participants with a previous diagnosis and those with elevated systolic or diastolic BP at the time of the study examination classified as cases. In addition, we estimated associations with prevalent hypertension based on a previous physician diagnosis only, after excluding participants with elevated BP at the study examination only. In order to compare with other ESCAPE cohorts, all of the estimated effects were uniformly presented as the mean and 95% confidence interval (CI) for BP values in increments of 10 $\mu g/m^3$ for PM_{10}, 5 $\mu g/m^3$ for $PM_{2.5-10}$ and $PM_{2.5}$, 10^{-5} m^{-1} for $PM_{2.5}$ absorbance, 20 $\mu g/m^3$ for NO_x, and 10 $\mu g/m^3$ for NO_2. We also estimated associations with IQR increases in the pollutants. An alpha level of 0.1, with a two-tailed distribution, was used to determine statistical significance for effect modification. All of the analyses were performed using SAS software (Version 9.1.3; SAS Institute).

Results

The basic characteristics of the 27,752 study subjects are summarized in Table 1. Our study population consisted of senior retired residents with a mean age of 74.8 years and a nearly equal gender distribution. 30.9% of study subjects had a BMI greater than 25 kg/m^2. Among 17,428 hypertensive subjects, 12,702 were self-reoprted physician-diagnosed hypertension and 4,726 belonged to measured unknown hypertension.

Table 2 shows the one-year average concentrations of six air pollutants for the 27,752 subjects. The annual average concentrations of NO_2 and PM_{10} were 23.7 $\mu g/m^3$ and 47.3 $\mu g/m^3$, respectively, which were below the National Ambient Air Quality Standards of the Taiwan Environmental Protection Agency (50 ppb for NO_2 and 65 $\mu g/m^3$ for PM_{10})

(http://ivy5.epa.gov.tw/epalaw/docfile/040060.pdf); however, the one-year average concentration of $PM_{2.5}$ (24.5μg/m^3) exceeded the National Ambient Air Quality Standards of Taiwan (15 μg/m^3 for $PM_{2.5}$). PM_{10} was moderately correlated to $PM_{2.5-10}$ (r=0.67), $PM_{2.5}$ (r=0.40), $PM_{2.5}$ absorbance (r=0.62), NO_x (r=0.53), and NO_2 (r=0.53) (See Supplemental Material, Table S2). PM_{10}, $PM_{2.5}$ absorbance, NO_x, and NO_2 were moderately correlated with the lengths of all major roads in a 25, 50, 100, and 500 m buffer zones (r=0.35-0.61).

We estimated statistically significant ($p < 0.05$) positive associations of average one-year exposures to PM_{10}, $PM_{2.5-10}$, $PM_{2.5}$ absorbance, NO_x, and NO_2 with diastolic BP, which were consistent among the different model specifications (Table 3). In the crude model, one-year exposures to PM_{10}, $PM_{2.5-10}$, $PM_{2.5}$ absorbance, NO_x, and NO_2, were associated with higher diastolic BP. After adjusting for individual covariates (main model), diastolic BP was associated with one-year exposures to air pollution, with estimates 0.73 (95% CI: 0.44, 1.03), 0.46 (95% CI: 0.30, 0.63), 0.62 (95% CI: 0.24, 0.99), 0.34 (95% CI: 0.19, 0.50), and 0.65 (95% CI: 0.44, 0.85) mmHg with increments of 10 μg/m^3 for PM_{10}, 5 μg/m^3 for $PM_{2.5-10}$, $10^{-5}m^{-1}$ for $PM_{2.5}$ absorbance, 20 μg/m^3 for NO_x, and 10 μg/m^3 for NO_2, respectively. The magnitudes of associations between diastolic BP and an interquartile range increment of PM_{10}, $PM_{2.5-10}$, $PM_{2.5}$ absorbance, NO_x, and NO_2, were 0.29-0.49 mmHg in the extended model (See Supplemental Material, Table S3). Diastolic BP also was positively associated with air pollutants (other than $PM_{2.5}$) after further adjustment for proximity to traffic (Table 3, extended model). Diastolic BP was not associated with $PM_{2.5}$ mass concentration in crude or adjusted models. In addition, none of the air pollutants was significantly associated with systolic BP (Table 3 and Supplemental Material, Table S3).

Figure 1 illustrates the associations between diastolic BP and PM_{10}, $PM_{2.5-10}$, and $PM_{2.5}$ absorbance stratified by an individual's comorbidities, including hypertension, diabetes, or obesity. We found 0.95 mm Hg (95% CI: 0.50, 1.40), 1.33 mm Hg (95% CI: 0.51, 2.15), and 0.99 mm Hg (95% CI: 0.50, 1.48) increase in diastolic BP for an increment of 10 $\mu g/m^3$ for PM_{10} in subjects with hypertension, diabetes, or a BMI $\geq$ 25 kg/m^2, respectively, which were higher than the values for subjects without hypertension [0.55 mm Hg (95% CI: 0.15, 0.94)], diabetes [0.64 mm Hg (95% CI: 0.32, 0.96)], or a BMI <25 kg/m^2 [0.59 mm Hg (95% CI: 0.22, 0.97)]. The p-values for interaction of hypertension, diabetes, and obesity with PM_{10} in the model were 0.03, 0.06, and 0.07, respectively. Similar results of stratified analyses results were observed for the association of $PM_{2.5}$ absorbance with diastolic BP. The p-values for interaction of the three comorbidity categories with $PM_{2.5}$ absorbance were 0.08, 0.03, and 0.01, respectively. The increase in diastolic BP with exposure of $PM_{2.5-10}$ was also higher in subjects with hypertension than without hypertension (p-value of interaction: 0.07), but associations were only slightly stronger among those with diabetes or obesity (interaction p-values 0.17 and 0.27, respectively). The associations between diastolic BP and NO_x or NO_2 did not differ according to comorbidity categories (data not shown). Estimates of associations with systolic or diastolic BP stratified according to a previous diagnosis of hypertension (n = 12,702) versus no previous history of hypertension (n = 15,050, including participants with elevated systolic or diastolic BP at the study examination) (Supplemental Material, Table S4) were generally consistent with stratum-specific estimates when hypertension also included participants with elevated SBP or DBP at the study examination but no history of physician-diagnosed hypertension (as shown for selected exposure and diastolic BP in Figure 1).

Table 4 shows the odd ratios of hypertension prevalence with one-year exposures to PM and nitrogen oxides. For both of main and extended models, we did not find any associations between prevalence of hypertension and one-year exposures to air pollution in the 27,752 subjects enrolled in the study. Still, no associations were found between hypertension and air pollution in the subset of 23,026 participants from which subjects belonged to measured unknown hypertension were excluded to consider the misclassification of hypertension by BP measurement error.

Discussion

Our study results demonstrate a positive association between diastolic BP and one-year exposures to air pollution among people over the age of 65 by use of the large study population and the comprehensive residential address information to improve the estimation of annual average air pollution exposures. In addition, associations of PM_{10}, $PM_{2.5-10}$, and $PM_{2.5}$abs were stronger among those with hypertension, diabetes, or obesity than among participants without these comorbid conditions. Although the point estimates were small and bias cannot be ruled out, they add to existing evidence suggesting that air pollution exposures may have a substantial public health impact, especially in vulnerable populations, given the ubiquitous nature of these exposures.

The annual average concentrations of PM_{10} and $PM_{2.5}$ for participants in this study were fairly high in comparison to those in other ESCAPE cohorts (Fuks et al. 2014). The positive findings in associations between different sizes in PM and diastolic BP may be attributable to high particulate concentrations in Taipei. Vehicular emissions and road dust are principle components of PM_{10} and $PM_{2.5-10}$ in the Taipei metropolitan area (Liang et al. 2013). Reflectance

measurements of $PM_{2.5}$ absorbance have been shown to correlate well with actual measurements of elemental carbon and can be considered to be a marker for traffic emissions ('diesel soot'). The exposure data in this study showed that $PM_{2.5}$ absorbance was correlated with the lengths of all major roads in 25, 50, 100, and 500 m buffer zones. This finding suggests that associations between diastolic BP and $PM_{2.5}$ absorbance may have been driven by effects of traffic-emitted $PM_{2.5}$ components. Hoffmann et al. (2009) found an association between residential traffic road proximity and decrease in ankle-brachial index. Schwartz et al. (2012) found significant positive associations between systolic BP, as well as diastolic BP and one-year averaged black carbon levels. These findings also support that traffic-emitted particles are key components relevant to cardiovascular health.

The role of the traffic-related pollution is further supported by the fact that we observed two other air pollutants, NO_x and NO_2, were also positively associated with diastolic BP. Previously, limited information was available on associations of NO_x and NO_2 with BP, and the results remain inconclusive. Bilenko et al. (2013) recently reported a positive association between long-term NO_2 and diastolic BP in children. Two other studies reported weak inverse associations between long-term exposures to NO_x and NO_2 and BP (Liu et al. 2014; Sørensen et al. 2012); whereas subgroup analyses in Sørensen et al. (2012) found 5-years exposure of NO_x was weakly but not significantly associated with systolic BP in subjects with past history of cardiovascular disease. In the ESCAPE analysis of more than 10000 participants, NO_2 showed a weak inverse relationship with systolic BP in non-medicated participants, but not in medicated participants (Fuks et al. 2014). More studies are therefore necessary to understand the relationships between NO_x and NO_2 and BP.

Furthermore, the stratified analyses found stronger associations between one-year PM_{10} and $PM_{2.5}$ absorbance exposures and BP among subjects with hypertension, diabetes, or obesity, which are three important determinants of metabolic syndrome. But we did not find any associations between $PM_{2.5}$ or any of the other exposures and systolic BP. Auchincloss et al. (2008) found 30-day exposures to $PM_{2.5}$ was associated with higher systolic BP and pulse pressure in subjects with hypertension or anti-hypertensive medication prescription. Some possible biomechanisms, including systemic inflammation, oxidative stress, and endothelial dysfunction, may contribute to the enhanced association between BP and long-term exposures to PM in these vulnerable subjects (Dubowsky et al. 2006; Brook and Rajagopalan 2009). Our findings suggest that these people are more vulnerable to long-term air pollution effects and should be well educated about the potential impacts of long-term air pollution exposures.

Previous studies reported a stronger association between BP and air pollution among subjects with anti-hypertensive medication (Auchincloss et al. 2008; Schwartz et al. 2012; Fuks et al, 2014). Although the information on anti-hypertensive medication was not available in our study, we believed that the study subjects who had history of physician-diagnosed hypertension should have been prescribed with anti-hypertensive medication, which has been mandatory for reimbursement under the implement of National Health Insurance in Taiwan since 1995. Therefore subgroup analyses stratified by self-reported physician-diagnosed hypertension may reflect the effect of anti-hypertensive medication on BP-air pollution relationship in our study (See Supplemental Material, Table S4). We found that estimates for diastolic BP with exposures to PM_{10}, $PM_{2.5\text{-}10,}$ and $PM_{2.5}$ absorbance were stronger in subjects with history of physician-diagnosed hypertension in comparison to subjects who denied a history of

physician-diagnosed hypertension. Such results were different from the findings by Fuks et al. (2014), who reported increase in BP in non-medicated participants. Our findings imply that the BP-air pollution relationship may be primarily modified by study subject's hypertensive status. Also, a rebound in BP may contribute to a higher diastolic BP response to air pollution among subjects with physician-diagnosed hypertension as participants were asked in advance not to take their antihypertensive medication in the morning when they came to do their physical examination.

In this study, we observed isolated elevations in diastolic BP, but not systolic BP, with one-year exposures to air pollution. Systolic BP is considered a major cardiovascular disease risk factor, especially in elderly. In general, there is a linear rise in systolic BP after age 30, but diastolic BP declines with age after age 50 to 60 (Franklin et al. 1997). The negative finding of the association between systolic BP and one-year air pollution exposures may be attributable to a much larger effect of traditional risk factor, e.g. age, on systolic BP than one-year air pollution exposures among our study subjects. Diastolic BP is, to some extent, associated with the trend of arterial resistance. The increase in diastolic BP may reflect the loss of elasticity as well as the progressive diffusion of atherosclerotic lesions with exposures to air pollution. Previous studies also suggested that isolated diastolic hypertension is associated with increased risk of specific cardiovascular disease, such as stroke, aortic aneurysm, or peripheral occlusive artery disease (Arima et al. 2011; Rapsomaniki et al. 2014). In addition, diastolic BP, a relatively stable component of the arterial sphygmogram, may be more likely to be associated with air pollution by one single BP measurement in this study. By contrast, systolic BP, which is considered as the dynamic component of BP and more closely linked to variations in pulse pressure, is more easily

influenced by study subject's short-term activity before measurements. A single measurement of systolic BP may result in wider variation than diastolic BP and bias the association between air pollution and systolic BP toward to null in this study.

Average one-year exposures to air pollution were not associated with the prevalence of hypertension in the present study. The definition of hypertension in this study was based not only on self-reported physician-diagnosed hypertension but also measured unknown hypertension; however, the single measurement of BP values may have led to a false positive assignment of hypertension. Such misclassification most likely biased the results. Still the associations between hypertension and one-year exposures to air pollutants were not found when subjects measured unknown hypertension were excluded. Another possible explanation for this null result is that the study population volunteered to participate in the health screening program and might be healthier than other elderly. Our study population had a comparatively higher educational attainment level and lower prevalence of health risk behaviors, i.e., alcohol consumption and smoking, than the age-matched population in Taiwan (Liang et al. 2004). This "healthy survivor effect" may bias the effect estimates towards to the null.

Several limitations of our study should be noted. We did not control the individual or neighborhood levels of socioeconomic status. In general, education, occupation, and income are considered important determinants for socioeconomic status. We controlled the education attainment, but did not control occupation and income due to the lack of relevant information in our data. However, the effect of occupation on health behaviors could be ignored as our study subjects were all aged over 65 years, the mandatory retirement age in Taiwan. On the other hand, some studies found insignificant effects on individuals' health by income equivalent scales in

Taiwan since the implementation of National Health Insurance in 1995, especially in the elderly (Leon-Gonzales and Tseng 2011; Hsiao and Cheng 2013). Therefore, we believe that education attainment is the best available indicator of socioeconomic status in our study. Another possible unmeasured confounder is traffic noise because noise has been demonstrated to be associated with increased BP and other cardiovascular outcomes (Babisch 2006; Chang et al. 2007). However, associations between diastolic BP and air pollutants did not change substantially with adjustment for traffic proximity, an important predictor for traffic noise modeling (Chang et al. 2012). Additionally, neither time-activity of the participants nor vertical distance of residency were considered in this study. The information on time spent indoors or type of residential ventilation was not available in this study. The fact that air pollution exposures for subjects who lived in mid- to high-level buildings (4^{th} floor or higher) can be overestimated up to 2 times for PM and 1.5 times for nitrogen oxides (Chu et al. 2012; Wu et al. 2014) by our LUR models, that may probably result in exposure misclassification. Lastly, because the study subjects were all over the age of 65 and from a single geographical area, additional investigations are needed to confirm whether the study results can be extrapolated to younger populations and people in different geographical areas.

Regardless of these limitations, average one-year exposures to PM (other than $PM_{2.5}$) and nitrogen oxides were associated with higher diastolic BP among Taipei City residents over 65 years of age. In addition, associations of diastolic BP with PM_{10} and $PM_{2.5}$ absorbance were stronger among those with hypertension, diabetes, or obesity than among participants without these comorbid conditions. Further cohort studies with repeated measures are necessary to confirm the casual relationship between long-term air pollution and changes in blood pressure.

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Table 1. Basic characteristics of study population (n=27,752).

Variable	Mean ± SD or n (%)
Age (years)	74.8 ± 6.4
Body mass index (kg/m^2)	24.3 ± 3.4
Systolic blood pressure (mm Hg)	136.3 ± 17.6
Diastolic blood pressure (mm Hg)	76.8 ± 10.2
Male sex; no. (%)	14414 (51.9)
Education Level	
Low (Primary school or less)	9585 (34.5)
Medium (Up to secondary school or equivalent)	10103 (36.4)
High (University degree and more)	8064 (29.1)
Alcohol consumption	
<1 drink/week	22205 (80.0)
1 to 3 drinks/week	4972 (17.9)
>3 drinks/week	575 (2.1)
Smoking	
Current smoker	1868 (6.7)
None-current smoker	25584 (93.3)
Physical activity	
<1 hour/week	16795 (60.5)
1 to 3 hours/week	8160 (29.4)
>3 hours/week	2792 (10.1)
Hypertension	17428 (62.8)
Physician-diagnosed hypertension[a]	12702 (45.8)
Measured unknown hypertension[b]	4726 (17.0)
Diabetes[c]	3557 (12.8)

[a]Physician-diagnosed hypertension was defined as subjects had been diagnosed with hypertension and use of anti-hypertensive medication. [b]Measured unknown hypertension was defined as subjects with measured BP values equal to or higher than 140 mm Hg for systolic BP or 90 mm Hg for diastolic BP but had never been diagnosed with hypertension. [c]Diabetes was defined as physician-diagnosed diabetes and use of anti-diabetic medication or fasting glucose over 126 mg/dl in the health examination.

Table 2. One-year average concentrations of six air pollutants for 27,752 subjects.

Exposures	Mean ± SD	IQR	Range
PM_{10} ($\mu g/m^3$)	47.3 ± 4.0	5.3	(36.1-63.9)
$PM_{2.5-10}$ ($\mu g/m^3$)	21.2 ± 3.5	5.2	(15.9-33.9)
$PM_{2.5}$ ($\mu g/m^3$)	24.5 ± 3.9	4.0	(12.8-48.2)
$PM_{2.5}$ absorbance ($10^{-5}m^{-1}$)	1.8 ± 0.3	0.4	(1.1-3.1)
NO_x ($\mu g/m^3$)	38.4 ± 15.3	17.5	(0.1-78.7)
NO_2 ($\mu g/m^3$)	23.7 ± 5.8	6.7	(4.2-37.2)

Table 3. Associations of systolic and diastolic blood pressures with annual averages of particulate matter and nitrogen oxides.

Exposures (increment)	Models	Systolic BP	Diastolic BP
		mm Hg (95% CI)	mm Hg (95% CI)
PM_{10} (10 μg/m^3)	Crude	0.21 (-0.31, 0.73)	0.75 (0.45, 1.05)
	Main	0.33 (-0.17, 0.84)	0.73 (0.44, 1.03)
	Extended	0.45 (-0.08, 0.99)	0.77 (0.46, 1.09)
$PM_{2.5-10}$ (5 μg/m^3)	Crude	-0.11 (-0.40, 0.19)	0.50 (0.33, 0.67)
	Main	-0.03 (-0.31, 0.26)	0.46 (0.30, 0.63)
	Extended	-0.01 (-0.30, 0.28)	0.46 (0.29, 0.63)
$PM_{2.5}$ (5 μg/m^3)	Crude	-0.01 (-0.28, 0.25)	-0.09 (-0.24, 0.06)
	Main	0.08 (-0.17, 0.34)	-0.02 (-0.18, 0.13)
	Extended	0.11 (-0.15, 0.38)	-0.05 (-0.20, 0.11)
$PM_{2.5}$ absorbance (10^{-5} m^{-1})	Crude	-0.06 (-0.73, 0.60)	0.72 (0.34, 1.10)
	Main	0.15 (-0.49, 0.78)	0.62 (0.24, 0.99)
	Extended	0.26 (-0.41, 0.94)	0.63 (0.23, 1.03)
NO_x (20 μg/m^3)	Crude	-0.16 (-0.43, 0.11)	0.33 (0.17, 0.49)
	Main	-0.00 (-0.26, 0.26)	0.34 (0.19, 0.50)
	Extended	0.07 (-0.23, 0.37)	0.41 (0.23, 0.59)
NO_2 (10 μg/m^3)	Crude	-0.04 (-0.40, 0.31)	0.65 (0.45, 0.86)
	Main	0.17 (-0.18, 0.51)	0.65 (0.44, 0.85)
	Extended	0.28 (-0.10, 0.66)	0.74 (0.52, 0.97)

The main models were calculated by generalized linear models, adjusted for sex, age, age mean-centered square, BMI, BMI mean-centered square, smoking status, alcohol consumption, education, hypertension, and diabetes. The extended models were further adjusted for traffic proximity in addition to covariates in the main models.

Table 4. Estimated odd ratios for the prevalence of hypertension with one-year exposures to particulate matter and nitrogen oxides.

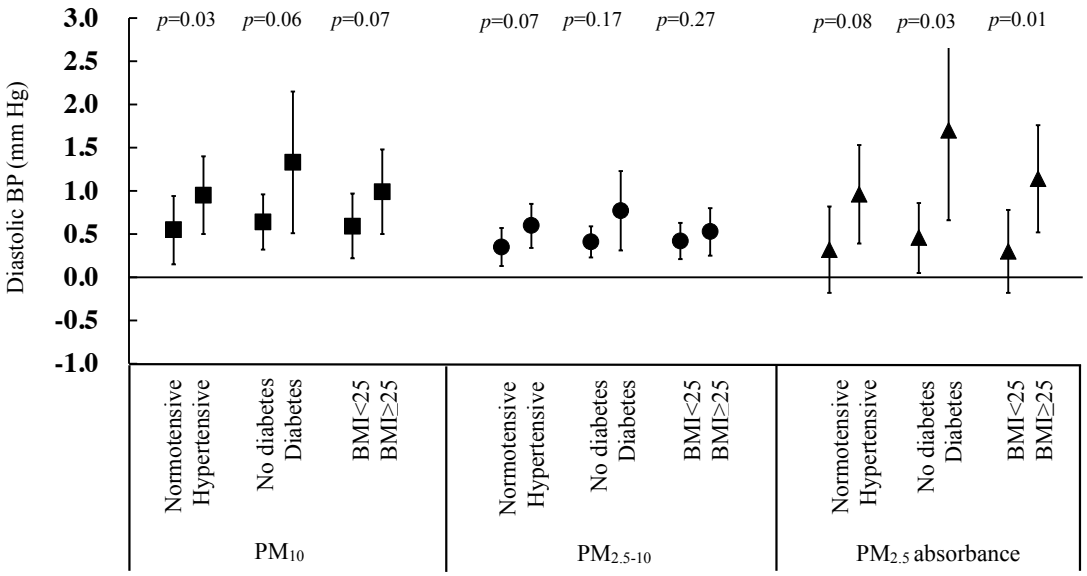
Exposures (increment)	Models	All subjects (n=27,752)	Measured unknown hypertension excluded (n=23,026)
		Odd ratio (95% CI)	Odd ratio (95% CI)
PM_{10} (10 μg/m^3)	Main	1.000 (0.939, 1.066)	0.983 (0.917, 1.054)
	Extended	1.001 (0.936, 1.071)	0.976 (0.907, 1.051)
$PM_{2.5-10}$ (5 μg/m^3)	Main	0.996 (0.961, 1.033)	1.003 (0.964, 1.043)
	Extended	0.997 (0.961, 1.033)	1.002 (0.963, 1.042)
$PM_{2.5}$ (5 μg/m^3)	Main	0.991 (0.959, 1.023)	0.976 (0.942, 1.011)
	Extended	0.991 (0.958, 1.024)	0.972 (0.937, 1.009)
$PM_{2.5}$ absorbance (10^{-5} m^{-1})	Main	0.926 (0.854, 1.003)	0.921 (0.842, 1.001)
	Extended	0.918 (0.843, 1.001)	0.917 (0.835, 1.001)
NO_x (20 μg/m^3)	Main	0.990 (0.958, 1.023)	0.978 (0.944, 1.014)
	Extended	0.988 (0.951, 1.026)	0.967 (0.927, 1.009)
NO_2 (10 μg/m^3)	Main	0.999 (0.956, 1.043)	0.987 (0.941, 1.034)
	Extended	0.999 (0.952, 1.048)	0.979 (0.929, 1.032)

The main models were calculated by logistic regression models, adjusted for sex, age, age mean-centered square, BMI, BMI mean-centered square, smoking status, alcohol consumption, education, and diabetes. The extended models were further adjusted for traffic proximity in addition to individual covariates in the main models.

Figure Legend

Figure 1. Estimates (95% CIs) of diastolic blood pressure in association with an increment of 10 $\mu g/m^3$ for PM_{10}, 5 $\mu g/m^3$ for $PM_{2.5-10}$, and $10^{-5}m^{-1}$ for $PM_{2.5}$ absorbance stratified by hypertensive (physician-diagnosed hypertension or measured unknown hypertension), diabetic (physician-diagnosed diabetes and use of anti-diabetic medication or fasting glucose over 126 mg/dl in health examination), or obese (BMI $\geq$ 25 kg/m^2) status. The estimates were calculated by generalized linear models, adjusted for sex, age, age mean-centered square, smoking status, alcohol consumption, education, traffic proximity, and individual comorbid conditions other than analyzed stratum.

Figure 1


Diastolic BP (mm Hg)
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
p=0.03
p=0.06
p=0.07
p=0.07
p=0.17
p=0.27
p=0.08
p=0.03
p=0.01
Normotensive
Hypertensive
No diabetes
Diabetes
BMI<25
BMI≥25
PM10
PM2.5-10
PM2.5 absorbance